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Meta-Analysis of predictive symptoms for Ebola virus disease in West Africa

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Background: One of the leading challenges in the West African Ebola virus disease (EVD) outbreak in 2014/15 was how best to quickly identify patients with Ebola, separating them from those without the disease. This meta-analysis aggregates all available data on symptom predictors for Ebola. This will enable quicker diagnosis of probable cases in resource-limited settings, and earlier stratification of patients as high-risk, permitting appropriate clinical and public health precautions to be taken.

Methods & Materials: Identification of relevant existing literature was performed by an online search in MEDLINE and EMBASE for studies published from 1st January 1946 to 11th September 2017. The MESH headings (keywords) included "ebola" and "symptom*" or "clinical" or "predict*" or "suspect*". The initial search on MEDLINE and EMBASE produced 4380 results. After exclusion criteria and further review, there were seven papers that met our criteria.

For each predictive symptom investigated, EVD and non-EVD patients were aggregated across studies. We then used a random effects meta-analysis model in STATA. This provided a pooled odds ratio along with 95% confidence intervals and a p-value, for each symptom; with detailed forest plots.

Results: Fatigue was the most predictive for Ebola (OR 3.29, 95% CI 1.89-5.71), with anorexia (OR 3.11, 95% CI 1.40-6.94), confusion (OR 3.04, 95 CI 2.18-4.23) diarrhoea (OR 3.02, 95% CI 1.89-4.85), conjunctivitis (OR 2.99, 95% CI 1.77-5.04), vomiting (OR 2.89, 95% CI 1.79-4.67), fever (OR 2.37, 95% CI 1.33-4.21), hiccups (OR 2.25, 95% CI 1.23-4.08) and dysphagia (OR 2.22, 95% CI 1.18-4.18) all more than twice as likely in Ebola cases. Chest pain, bleeding, and sore throat were not statistically significant predictors of Ebola.

Conclusion: Existing literature fails to provide a unified position on the most predictive symptoms for Ebola. This analysis demonstrates that late presenting symptoms including confusion, anorexia, conjunctivitis and hiccups are predictive for Ebola. However, early non-specific symptoms of fatigue, fever, diarrhoea, vomiting were also highly predictive. These findings will aid effective future clinical assessment, risk stratification tools and emergency epidemic response.

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Impact of 4% deltamethrin-impregnated dog collars on the incidence of human visceral leishmaniasis

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Background: In Brazil, visceral leishmaniasis (VL) is caused by the protozoan parasite *Leishmania infantum*, primarily transmitted by the sand fly *Lutzomyia longipalpis* with the dog as the main urban reservoir. This study aims to evaluate the effectiveness of 4% deltamethrin-impregnated dog collars (DMC) on the incidence of human visceral leishmaniasis (HVL).

Methods & Materials: This is a cluster randomized trial carried out in 6 municipalities in Brazil. In each municipality, two areas were randomly allocated to either (1) culling seropositve dogs + residual insecticide spraying (control area - CA) or (2) culling seropositve dogs + residual insecticide spraying + DMC fitted to dogs every six months during two years (intervention area - IA). The study started in the second semester of 2012. Cases of HVL (n = 1167) occurring from 2008 to 2015 were identified from the Brazilian Reportable Diseases Information System and georeferenced to control and intervention areas of each municipality. HVL cases from 2008 to 2012 were considered as occurring in the "pre-intervention" period, and those from 2013-2015 occurring in the "post-intervention" period. We used a mixed-effects Poisson regression model to estimate the effectiveness of the intervention comparing the changes from pre to post intervention periods in the control and intervention areas.

Results: There was a statistically significant reduction in the incidence of HVL in both areas comparing the pre and post-intervention periods. However, the reduction was significantly higher in the intervention area yielding an effectiveness estimate of the DMC of 27% (IC95% 2%-46%, p = 0.036).

Conclusion: The use of DMC was associated with a reduction of 27% in the incidence of HVL, suggesting that DMC could be used as an additional strategy form controlling visceral leishmaniasis in Brazil. However, since the estimate of the effectiveness is relatively small and DMC are expensive, a cost-effectiveness analysis should be performed before recommending a large scale introduction of such preventive device.

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